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21 June 2019

Version of attached file:

Accepted Version

Peer-review status of attached file:

Peer-reviewed

Citation for published item:

Vera, Jesús and Raimundo, Jiménez and García-Durán, Beatriz and Pérez-Castilla, Alejandro and Redondo, Beatriz and Delgado, Gabriel and Koulieris, George-Alex and García-Ramos, Amador (2019) 'Acute intraocular pressure changes during isometric exercise and recovery : the influence of exercise type and intensity, and participants sex.', *Journal of sports sciences.*, 37 (19). pp. 2213-2219.

Further information on publisher's website:

<https://doi.org/10.1080/02640414.2019.1626072>

Publisher's copyright statement:

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Title: Acute intraocular pressure changes during isometric exercise and recovery: the influence of exercise type and intensity, and participant's sex.

Running head: IOP behavior during isometric effort and recovery

Abstract

Objectives: To evaluate the intraocular pressure (IOP) behaviour during a 1-minute period of isometric physical effort and the immediate 1-minute of recovery in the mid-thigh clean pull and squat exercises at three different intensities.

Methods: Twenty physically active individuals performed the isometric mid-thigh clean pull and squat exercises at three intensities (0% [low-intensity], 25% [medium-intensity] and 50% [high-intensity] of the maximum isometric force). IOP was semi-continuously measured by rebound tonometry, and these values were processed to obtain a continuous IOP signal.

Results: There was a statistically significant effect of exercise intensity on IOP ($p < 0.001$, $\eta_p^2 = 0.416$), observing that IOP increments were positively associated with exercise intensity. The mid-thigh clean pull and squat exercises did not demonstrate differences ($p = 0.510$), and also, no differences were observed between men and women ($p = 0.683$). The IOP changes during the isometric physical effort showed a positive linear behaviour in all conditions ($r = 0.70$ to 0.96). IOP returned to baseline levels after 8 seconds of recovery.

Conclusions: Our data showed a progressive and instantaneous IOP increment during isometric exercise, which was positively associated with exercise intensity. IOP changes were independent on the type of exercise and participant's sex. After exercise, IOP rapidly (≈ 8 seconds) returned to baseline levels.

Keywords: strength training; mid-thigh clean pull; squat; glaucoma management; exercise intensity.

Introduction

Recent recommendations of the Physical Activity Guidelines Advisory Committee highlight that regular practice of physical exercise promotes a variety of health benefits, including a reduced risk of cancer and fall-related injuries, as well as an improved bone, cardiovascular and brain health among others (Piercy et al., 2018). The combination of aerobic and muscle-strengthening exercises has been generally recommended for individuals with chronic health conditions (Piercy et al., 2018). Within this range of medical conditions, those related to the eye health have gained attention in the last years (Wylegala, 2016). Of special note is the role of physical exercise in the management and prevention of glaucoma, since this ocular condition is the leading cause of irreversible blindness worldwide (Tham et al., 2014). The reduction and stabilization of intraocular pressure (IOP) are the only proven strategies for the management of glaucoma (The AGIS Investigators, 2010). The acute and long-term adaptations induced by exercise demonstrably modulate IOP levels, whereas the prevailing direction of these IOP changes depends on exercise and participant's characteristics (Zhu et al., 2018).

In relation to the different moderating factors on the impact of physical exercise on IOP, the type of physical exercise is evidently very relevant. Physical exercise performed without overload seems to promote an IOP reduction during exercise, as manifested for different physical activities such as cycling at moderate intensities (Najmanova, Pluhacek, & Botek, 2016) or performing a high intensity interval training (Vera, Jiménez, Redondo, Cárdenas, et al., 2018). Contrary, the execution of physical efforts against external resistances (e.g., strength exercise) or sport disciplines such as yoga have showed to induce an acute IOP increment (Jasien, Jonas, De Moraes, & Ritch, 2015; Rüfer et al., 2014; Vieira, Oliveira, de Andrade, Bottaro, & Ritch, 2006). In particular, weightlifting training performed both in a dynamic and isometric manner demonstrably raises IOP levels (Bakke, Hisdal, & Semb, 2009; Vera, Jiménez, Redondo, Torrejón, et al., 2018). While the IOP changes induced by dynamic resistance training have been positively associated with the overload used or the level of effort accumulated (Vera, Jiménez, Redondo, Torrejón, et al., 2018; Vera, Garcia-Ramos, Jiménez,

& Cárdenas, 2017), previous studies focusing on isometric resistance training have found acute IOP increments when adopting a squat position without exerting force (Castejon et al., 2010) or when participants are asked to exert force by squeezing a grip with the right hand (Bakke et al., 2009). Few studies have focused on the impact of isometric effort on IOP and, importantly, no study has investigated the influence of exercise intensity on IOP during isometric resistance training conditions, as well as possible variations between commonly used isometric resistance training exercises. This information would be of interest to assess the mediating role of exercise intensity and exercise type during isometric efforts on IOP.

Most studies have focused on the assessment of IOP variations during exercise, however, the time needed for IOP levels to recover has been scarcely investigated. For example, Najmanova et al. (Najmanova et al., 2016) found that IOP variations induced by exercise (cycling at moderate intensity for 30 minutes) lasted ten minutes after the exercise ceased. However, results related to the resistance training seem to agree that IOP rapidly returns to baseline levels (Vera, Jiménez, Redondo, Torrejón, et al., 2018). The assessment of IOP during physical effort and recovery periods would allow us to clarify how IOP behaves during and after physical effort. Additionally, it is broadly-accepted that there are physiological differences between men and women, with females being commonly under-represented in the sports and exercise medicine research (Costello, Bieuzen, & Bleakley, 2014). Recent scientific evidence has found a different IOP behavior during high-intensity interval-training between men and women (Vera, Jiménez, Redondo, Cárdenas, et al., 2018), although, these sex differences have not yet been tested during resistance training efforts. Therefore, we consider that the comparison between men and women would help to expand our knowledge in this regard.

In view of the gaps identified in the scientific literature, the present study aimed to: (i) semi-continuously assess the IOP behavior during a period of 1-minute isometric resistance training effort, as well as during a period of 1-minute after exercise cessation, (ii) to determine the influence of the type of exercise (mid-thigh clean pull and squat) and the exercise intensity (0%, 25%, and 50% of the

maximum isometric voluntary strength), and (iii) to explore the possible differences between men and women. The isometric mid-thigh clean pull and squat exercises were chosen because they are two exercises commonly used to evaluate and develop the strength of lower-body muscles due to their similarity with many sport activities (Schoenfeld, 2010; Wang et al., 2016). Based on previous studies, we hypothesized that (i) IOP would progressively increase during isometric resistance training conditions, and then gradually recover back to baseline levels following the physical effort (Bakke et al., 2009; Castejon et al., 2010), (ii) greater exercise intensities would promote a higher IOP increment, as shown during dynamic strength exercise (Vera, Garcia-Ramos, et al., 2017), however, the lack of studies comparing between exercises does not allow us to establish a hypothesis for the possible role of the type of exercise, and (iii) the effect of physical effort on IOP would not differ between men and women as it has been reported during dynamic resistance training (Vera et al., 2019).

Methods

Participants and ethical approval

Twenty physically active young adults (10 women and 10 men) participated in this study (see Table 1 for sample characteristics). All participants were free of any systemic or ocular disease, and had at least two years of recreational experience with resistance training. Additionally, they were asked to avoid any strenuous exercise two days prior to each testing session, as well as to refrain from alcohol or caffeine consumption 12 hours before attending to the laboratory. The present study was conducted in conformity with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and the experiment was carried out under the guidelines of the university Institutional Review Board (IRB approval: 546/CEIH/2018).

Procedure

Participants attended to the laboratory in two occasions separated by a minimum of 48 h. The first session was used for anthropometrical measures as well as to determine the maximum isometric strength in mid-thigh clean pull and squat exercises (see below for further details). The second session consisted of an isometric squat and mid-thigh clean pull protocol against three relative intensities (0%, 25%, and 50% of the maximum isometric strength) applied in randomized order. The vertical ground reaction force (VGRF) for the 25% (i.e., medium intensity) and 50% (i.e., high intensity) of maximum isometric strength was 977.0 ± 147.5 N and 1230.8 ± 260.7 N for the mid-thigh clean pull, and 975.7 ± 185.4 N and 1239.1 ± 298.0 N for the squat exercise, respectively. Only one trial was performed for each loading condition (a total of six series) and a rest period of 10 min was imposed between successive trials. Before the commencement of the main experimental session, we obtained baseline IOP levels for each participant. Afterwards, participants had to achieve the required exertion and maintain constant tension during a 1-min period. A computer screen placed in front of the participants and at eye level allowed them to receive visual feedback of the force-time trace using the force platform software (BioWare v. 5.3.0.7, Kistler, Switzerland), while an experienced optometrist simultaneously measured the IOP (see **Figure 1** for a schematic illustration). When the isometric effort ended, participants adopted a standing position without producing any exertion and IOP was measured during the immediate subsequent 1-min recovery period. Participants were instructed to avoid the Valsalva maneuver, which has showed to promote an IOP increment (Aykan, Erdurmus, Yilmaz, & Bilge, 2010).

Maximal isometric strength assessment and data acquisition

Participants performed a standardized warm-up, which consisted of jogging, self-selected dynamic stretching and joint mobilization exercises, followed by three sustained contractions for 3-4 s at 20, 40, 60 and 80% of maximal perceived exertion. Subsequently, they performed 2 maximal isometric efforts lasting 3-5 s. Resting periods between efforts were set to 3 min. Participants were instructed

to pull or push the bar “as fast and as hard as possible” during the mid-thigh clean pull and squat protocol, respectively. A rest period of 5 min was given between isometric protocols. The order of each protocol was randomized between participants.

The isometric mid-thigh clean pull and squat protocols required participants to position themselves on a force platform inside of a Smith machine (Life Fitness, Victoria, Australia) that allowed fixation of the bar at any height. During the isometric squat exercise, the bar height was adjusted to achieve a squatted position with an internal knee angle of approximately 90° (Bazyler, Beckham, & Sato, 2015), while for the isometric mid-thigh clean pull exercise the bar height was adjusted to the participants’ second pull position of the power clean with an external knee and hip angles of approximately 140° (James, Roberts, Haff, Kelly, & Beckman, 2017). The individual knee and hip angles were independently measured with a hand-held goniometer in order to ensure positions were replicated in each isometric effort.

The vertical ground reaction force (VGRF) produced was recorded by a force platform (9260 AA, Kistler, Switzerland) on which the participants’ feet were placed during each isometric effort. The position of the feet was recorded for subsequent efforts. The VGRF was sampled at 50 Hz and displayed on the screen situated in front of the athletes.

Intraocular pressure assessment and data processing

A portable rebound tonometer was used to assess IOP (Icare, TiolatOy, INC. Helsinki, Finland) in the right eye. This instrument has been clinically validated (Pakrou, Gray, Mills, Landers, & Craig, 2008) and employed in related research (Rüfer et al., 2014; Vera, Jiménez, et al., 2017). The main advantages of the Icare tonometer in comparison to others techniques (e.g., Goldman applanation tonometry) include: (i) it is portable and hand-held, (ii) it can rapidly measure IOP, (iii) the procedure is well-tolerated and (iv) measuring does not require the use of topical anaesthesia. The inherent characteristics of the tonometer and the exercise (static exercise with neutral neck position) allowed us to semi-continuously measure IOP. This constitutes the main novelty of this investigation,

since previous studies have commonly tested the short-term effects of physical exercise on IOP in a simple pre/post design (Rüfer et al., 2014; Vera, Jiménez, Redondo, Cárdenas, & García-Ramos, 2018; Vera, Jiménez, et al., 2017; Vera, Garcia-Ramos, et al., 2017; Vieira et al., 2006). While exercising, participants were instructed to fixate on a distant target as consecutive measurements were taken against the central cornea. Every six measurements, the mean value is displayed, and the examiner vocalized the IOP value to a research assistant for data logging. During the 1-minute isometric exercise as well as during the 1-minute recovery period, the examiner acquired IOP values in a continuous fashion. Due to (i) the tonometer's inability to acquire IOP measurements at exact time intervals, (ii) the lack of exact timestamps for the measurements and (iii) the manual logging of the values, we describe a process to overcome these technical restrictions and obtain a set of equally distributed values at regular intervals with exact timestamps.

We developed a procedure to obtain a set of equally distributed IOP measurements at regular intervals, thus overcoming the timestamping and lack of automatic logging restrictions of the rebound tonometer, described above. We based our method on multi-rate digital signal processing, in particular sample-rate conversion which is the process of changing the sampling rate of a discrete sampled signal to obtain a new discrete representation of the underlying continuous signal, in this case the IOP signal (Crochiere & Rabiner, 1983). IOP is a continuous function, as when IOP values rise and fall between two pressures, IOP will always take all intermediate values between those two pressures. In our process we treated the obtained samples as geometric points and create the necessary new points by polynomially interpolating those values, essentially approximating the source, continuous IOP signal, and then re-sampling at 15 discrete intervals for the 1-minute period, i.e., every 4 seconds.

Simply stated, when measuring IOP using the rebound tonometer, we sampled the continuous IOP function at slightly irregular intervals due to tonometer restrictions. The obtained values are the values of the IOP function at those moments-in-time. Yet due to the function being continuous we

can approximate the original IOP function from the sample measurements and then re-sample the derived function at specific, regular intervals, thus obtaining a fixed set of values at these exact intervals. The new data points are estimated within the range of the discrete set of sampled data points.

Statistical analysis

Before any statistical analysis, the normal distribution of the data (Shapiro-Wilk test) and the homogeneity of variances (Levene's test) were confirmed ($p > 0.05$). Then, a mixed analysis of variance (ANOVA) with the type of exercise (mid-thigh clean pull and squat), the exercise intensity (low, medium, high), the measurement moment (physical effort and recovery), and the point of measure (15 measurements) as within-participants factors, and with participant's sex (men and women) as the only between-participants factor, was performed for IOP. The magnitude of the differences was reported by the partial eta squared (η_p^2) and Cohen's d , as appropriate. Statistical significance was set at an alpha level of 0.05, and post hoc tests were corrected using the Bonferroni correction.

Results

Our analysis did not reveal statistically significant differences for the type of exercise ($F_{1, 18} = 0.451$, $p = 0.510$, $\eta_p^2 = 0.024$) and sex ($F_{1, 18} = 0.173$, $p = 0.683$, $\eta_p^2 = 0.010$), whereas the exercise intensity ($F_{2, 36} = 12.822$, $p < 0.001$, $\eta_p^2 = 0.416$), the measurement moment ($F_{1, 18} = 194.012$, $p < 0.001$, $\eta_p^2 = 0.915$) and the point of measure ($F_{14, 252} = 9.053$, $p < 0.001$, $\eta_p^2 = 0.335$) yielded statistical significance. There were also statistically significant differences for the interactive effects of *point of measure x sex* ($F_{14, 252} = 1.966$, $p = 0.021$, $\eta_p^2 = 0.098$), *exercise type x exercise intensity x sex* ($F_{2, 36} = 3.653$, $p = 0.036$, $\eta_p^2 = 0.169$), *type of exercise x measurement moment* ($F_{1, 18} = 30.052$, $p < 0.001$, $\eta_p^2 = 0.625$), *exercise intensity x measurement moment* ($F_{2, 36} = 24.604$, $p < 0.001$, $\eta_p^2 = 0.578$), *exercise intensity x measurement moment x sex* ($F_{2, 36} = 3.427$, $p = 0.043$, $\eta_p^2 = 0.160$), *type of exercise x point of measure* ($F_{14, 252} = 2.004$, $p = 0.018$, $\eta_p^2 = 0.100$), *exercise intensity x point of measure* ($F_{28, 504} = 1.801$, $p =$

0.008, $\eta_p^2 = 0.091$), *measurement moment x point of measure* ($F_{14, 252} = 14.290$, $p < 0.001$, $\eta_p^2 = 0.443$).

Post-hoc comparisons for the three exercise intensities showed significant differences between the high vs low (correct p-value = 0.002, Cohen's $d = 0.925$) and the medium vs low (corrected p-value = 0.001, Cohen's $d = 1.021$), whereas no differences were observed when the high and medium intensities were compared (corrected p-value = 0.340). Post-hoc comparisons for the three exercise intensities at each point of measure are depicted in Figure 2. No meaningful differences in IOP values were observed between men and women (**Figure 3**).

Discussion

Our data indicate that IOP is sensitive to isometric exercise, in particular exhibits a progressive IOP increment during effort. These changes were positively associated with exercise intensity, and independent on the type of exercise (mid-thigh clean pull and squat) and participant's sex. Although IOP values at the end of the isometric effort demonstrated increments ranging from 11% to 36%, IOP returned to baseline levels within the subsequent 8 seconds. These outcomes highlight that isometric exercise, mainly when highly demanding (against heavy loads or performing high relative force), may be undesirable for individuals with glaucoma, myopic fundus pathology or keratoconus where abrupt IOP fluctuations have to be prevented.

The present outcomes reveal that IOP increased as a function of the level of accumulated effort during isometric exercise, as we observed a strong positive association between IOP and time under tension. In this regard, a positive association between IOP levels and the level of accumulated effort has been recently found during dynamic strength exercise (Vera, Jiménez, Redondo, Torrejón, et al., 2018). We also found that producing more force during isometric exercise was associated with greater IOP increments. In our study, the average IOP peak during isometric effort reached increments up to 9 mmHg, and these changes were higher than those found with dynamic strength exercise (~ 5mmHg) (Vera, Jiménez, Redondo, Torrejón, et al., 2018). In comparison to the previous findings for isometric exercise, our results seem to indicate greater increments (~ 4 mmHg higher in our study),

although these differences may be the result of the type of exercise used by Bakke et al., (2009), as the handgrip exercise involves low muscle mass size. Based on our results, and as recommended in previous studies, we support the idea that exercise prescription for individuals with glaucoma should be carefully supervised by experts in physical exercise, and in collaboration with eye care specialists, since performing strength exercise in a dynamic or isometric manner promotes abrupt IOP variations that may have detrimental effects on ocular health (De Moraes, Mansouri, Liebmann, & Ritch, 2018).

The type of exercise has demonstrated to play a role on the IOP changes induced by physical effort, with more abrupt IOP changes in exercises involving greater muscle mass size or those exercises where the upper body is involved. For example, Rüfer et al., (2014) and Vera et al., (2017) have found that for exercises involving similar muscle size in the upper and lower body (butterfly vs. leg curl machines, and bench press vs. squat), greater IOP changes are obtained during strength training of the upper body. On the other hand, there is also evidence that exercises of the same body part, but with different muscle mass sizes (e.g., squat vs. calf raise), promote different IOP responses, with higher IOP increments in those with greater muscle size. For the two exercises compared in this study, we failed to find any difference between them. These results may be due to the similar muscle mass size and the part of body (lower body) involved in both exercises. We selected these two exercises as they are commonly prescribed in strength programs due to their transferability to athletic performance, however, future studies should include exercises involving different muscle mass size and body parts to explore their possible influence on IOP changes associated with isometric exercise.

One of the main results of this study is the rapid recovery (~ 8 seconds) of IOP after isometric effort, as demonstrated by the analysis of the IOP behavior on the immediate subsequent 1-minute period of recovery. These results evidence the transient effects of resistance exercise on IOP, with greater variations occurring during exercise. The IOP behavior during and after exercise seems to be exercise-dependent, with low-intensity aerobic exercise (cycling) inducing an IOP reduction that may last 10 minutes after exercise cessation (Najmanova et al., 2016), whereas resistance training

promotes acute IOP increments that quickly return to baseline levels after exercise (Vera et al., 2019). In view of this, the type of physical effort seems to play an important role on the IOP behavior during exercise and recovery. To date, most investigations have carried out pre/post designs to assess the impact of physical exercise on IOP, and thus, it seems plausible to expect that the available scientific literature has underestimated these effects. In addition, we consider that these IOP peaks associated with isometric efforts may be also relevant to other daily activities, mainly those that comprise interchanging gases (e.g., carrying a heavy shopping bag) (Baser, Karahan, Bilgin, & Unsal, 2018). Our data revealed a significant interaction between the type of exercise and measurement moment, observing greater IOP increments during the execution of the squat exercise in comparison to the mid-thigh clean pull, but lower IOP values for the squat in comparison to the mid-thigh clean pull during the recovery period (see Figure 2). This analysis evidences a more abrupt IOP variation immediately after ceasing isometric effort in the squat exercise when compared to the mid-thigh clean pull, which may be due to a physiological mechanism that try to reduce IOP levels by an accentuated aqueous humour drainage after acute IOP increments.

In addition, when testing for possible differences between sexes, our data did not reveal any differences between men and women. This finding is in agreement with dynamic strength exercise, in which no differences were observed between men and women (Vera, Jiménez, Redondo, Torrejón, et al., 2018). However, studies investigating sex-related differences in other physical-tasks without the use of external loads have found varying IOP responses between men and women (i.e., treadmill at 70% of peak oxygen uptake or high-intensity interval-training) (Dane, Koçer, Demirel, Ucok, & Tan, 2006; Vera, Jiménez, Redondo, Cárdenas, et al., 2018). We can firmly state, though, that both men and women suffer abrupt IOP changes during isometric effort, which rapidly return to baseline level after exercise completion. Nevertheless, the analysis of the interactive effects of sex revealed some differences between men and women. The IOP values obtained during isometric effort were generally higher for men in comparison to women (5 out of 6 ES; see Figure 2), while in recovery

women presented higher IOP values (4 out of 6 ESs; see Figure 3). Based on this, isometric effort promotes a similar IOP response between both sexes, however women seem to present a less accentuated IOP variation between the periods of isometric effort and recovery.

The present study is not exempt of limitations that must be acknowledged. First, our results are safely applicable to healthy young adults, as different findings may be observed for individuals of other age groups or with chronic health conditions. We encourage future studies to explore these findings in older population or glaucoma patients that have demonstrated an inefficient regulation of the aqueous humour dynamics (Gabelt & Kaufman, 2005). Second, the participant's fitness level has been shown to be a mediating factor on the IOP changes induced by dynamic strength exercise (Vera, Jiménez, Redondo, Cárdenas, et al., 2018), however, these effects have not been corroborated with isometric efforts, and thus, need further research. Third, participants were instructed to prevent the Valsalva Manoeuvre, since it demonstrably increases IOP levels (Aykan et al., 2010). Future studies should employ this respiration pattern during exercise in order to assess its influence on IOP. Fourth, both exercises were performed in standing position, however, body and head positions evidently affect IOP (Jasien et al., 2015; Prata, De Moraes, Kanadani, Ritch, & Paranhos, 2010). We hope that future studies will investigate the influence of body and head positions during isometric exercise. Lastly, we used a portable rebound tonometer to semi-continuously assess IOP during effort and recovery. Notably, a recent development of contact-sensors (SENSIMED Triggerfish, Lausanne, Switzerland) permits to continuously measure IOP (Mansouri, Weinreb, & Liu, 2015), although this technology may have several disadvantages for this experimental design. The contact-lens sensor is programmed to collect 300 data points during 30 seconds at 5 minutes intervals during 24 hours, and thus, it is not appropriate for the purposes of this study. Also, the contact-lens sensor output signal is given in arbitrary units for which no conversion into IOP values exists, and this method for IOP assessment has demonstrated a weak correlation with applanation tonometry (Vitish-Sharma et al., 2018). Further developments of this technology could enhance its usefulness in future investigations.

Summing up, an abrupt, rapid and progressive IOP increment occurs during isometric exercise, and this effect is more evident when exercising at greater intensities, with IOP returning to baseline levels within 8 seconds after the exercise has ceased. The mid-thigh clean pull and squat exercises induce similar IOP increments, and sex-related differences are inexistent. Our present outcomes support previous evidence on the detrimental effects of strength exercise when stable IOP levels are desirable. Our findings may be of interest for the management and prevention of glaucoma via lifestyle interventions, however, the external validity of these results for glaucoma patients needs to be addressed in future studies.

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Figure captions

Figure 1. Photographs of the study procedure during the isometric mid-thigh clean pull (Panel A) and squat (Panel B) exercises.

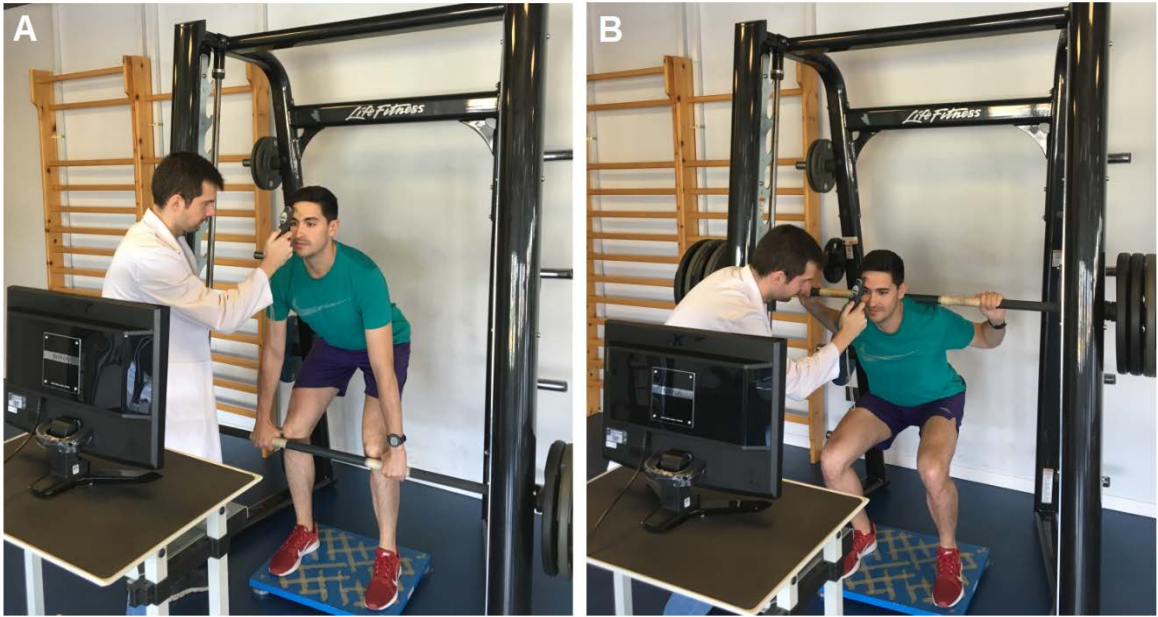


Figure 2. Effects of performing 1-minute of isometric mid-thigh clean pull (panel A) and squat (panel B) exercises at three different intensities. The recovery values represent the IOP measurements taken during the immediate subsequent 1-minute recovery period. *, # and \$ denote statistically significant differences for the comparisons high-intensity vs. low-intensity, high-intensity vs. medium-intensity, and medium-intensity vs. low-intensity, respectively.

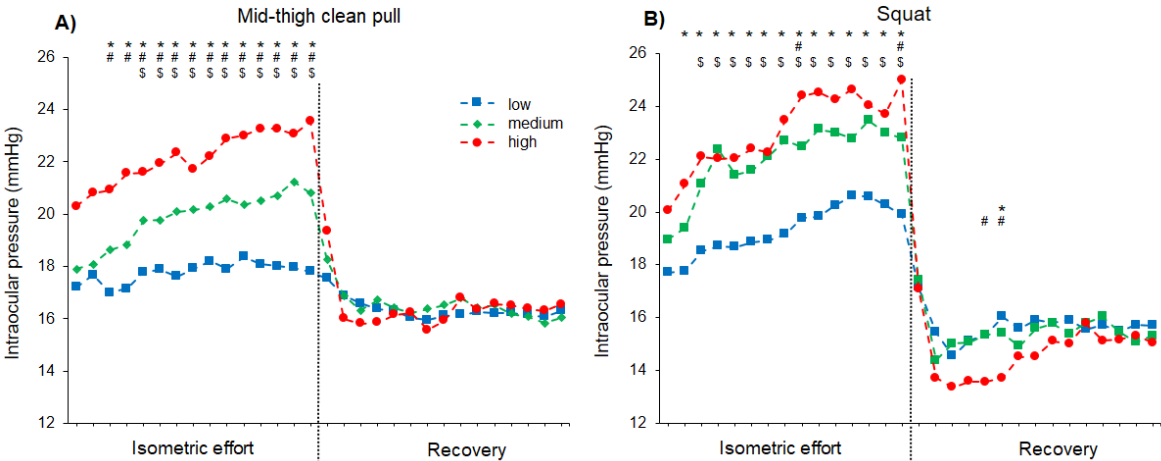


Figure 3. Standardized differences (Cohen's d effect size) in the intraocular pressure changes between men and women when performing the isometric mid-thigh clean pull (panel A) and squat (panel B) exercises at three different intensities. Error bars show the 90% confidence intervals.

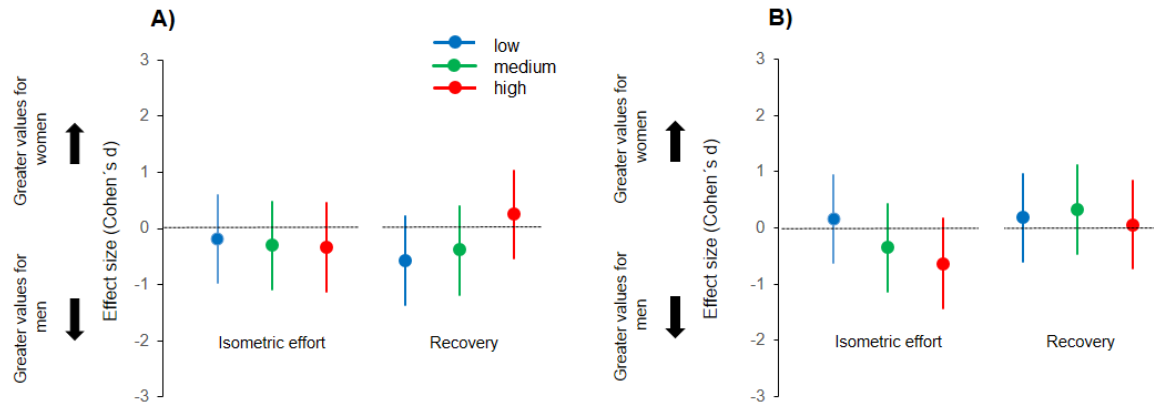


Table 1. Descriptive (mean \pm standard deviation) characteristics of the experimental sample.

	Total sample (n = 20)	Men (n = 10)	Women (n = 10)
Age (years)	23.8 \pm 3.1	24.2 \pm 3.0	23.4 \pm 3.2
Weight (kg)	68.4 \pm 7.2	78.4 \pm 8.2	58.4 \pm 6.2
Height (cm)	171.5 \pm 8.0	180.5 \pm 9.8	162.5 \pm 6.2